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Denaturation induced aggregation in α-crystallin: Differential action of chaotropes

Mohd Shahnawaz Khan, Mohammad A Alsenaidy and Abdulrahman M AlSenaidy
King Saud University, KSA

α-crystallin is a member of small heat shock proteins and is believed to play an exceptional role in the stability of eye lens proteins. The disruption or denaturation of the protein arrangement or solubility of the crystallin proteins can lead to vision problems including cataract. In the present study, we have examined the effect of chemical denaturants urea and guanidine hydrochloride (GdnHCl) on α-crystallin aggregation with special emphasis on protein conformational changes, unfolding and amyloid fibril formation. GdnHCl (4 M) induced a 16 nm red shift in the intrinsic fluorescence of α-crystallin, compared with 4 nm shift by 8 M urea suggesting a major change in α-crystallin structure. Circular dichroism analysis showed marked increase in the ellipticity of α-crystallin at 216 nm, suggesting gain in β-sheet structure in the presence of GdnHCl (0.5-1 M) followed by unfolding at higher concentration (2-6 M). However, only minor changes in the secondary structure of α-crystallin were observed in the presence of urea. Moreover, 8-anilinonaphthalene-1-sulfonic acid fluorescence measurement in the presence of GdnHCl and urea showed changes in the hydrophobicity of α-crystallin. Amyloid studies using thioflavin T fluorescence and Congo red absorbance showed that GdnHCl induced amyloid formation in α-crystallin, whereas urea induced aggregation in this protein. Electron microscopy studies further confirmed amyloid formation of α-crystallin in the presence of GdnHCl, whereas only aggregate-like structures were observed in α-crystallin treated with urea. Our results suggest that α-crystallin is susceptible to unfolding in the presence of chaotropic agents like urea and GdnHCl. The destabilized protein has increased likelihood to fibrillate.

moskhan@ksu.edu.sa